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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/615,285	07/12/2000	Daniel E. H. Afar	129.9US11	3235

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/615,285	AFAR ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,19,55 and 62-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11, 19, 55, 62-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Re: Afar *et al.*

Date of Priority: 04/14/1999

Request for Continued Examination

The request filed on 04/05/2004 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/615285 is acceptable and a RCE has been established. An action on the RCE follows.

Claims 11, 19, 55, 62-68 are pending.

Claim Objections

Claims 63, 65, and 67 are objected to for reciting "by contacting the sample with antibody or fragment thereof" which renders the claims grammatically unclear.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11,19 and 55 recite the limitation "said 20P1F12/TMPRSS2 gene products" in Claims 11, 19, and 55. There is insufficient antecedent basis for this limitation in the claim.

it would appear that the immunocomplex can be formed with "any" protein remotely resembling a 20P1F12/TMPRSS2 protein" whereas the independent claims clearly set forth that the 20P1F12/TMPRSS2 comprises SEQ ID NO:2.

Claims 63, 65, and 67 are rejected as vague for reciting "observing the presence or absence of an immunocomplex formed from the antibody or fragment with any 20P1F12/TMPRSS2 protein". Is it not clear what is encompassed by "any" 20P1F12/TMPRSS2 protein? Hence, the subject matter does not appear to be distinctly claimed and the metes and bounds of the claims cannot be determined.

Claims 11, 19, and 55 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is: a measurement or contact step which clearly implements the claimed examination of the level of expression of the 20P1F12/TMPRSS2 gene product as set forth in step (a) of the Claims. In other words, it is not distinctly clear how the gene levels are in fact examined. This rejection can be obviated by amending the claims to incorporate the subject matter of Claims 63, 65, and 67.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11, 19, 55, and 62-68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to a method for detecting evidence of prostate cancer by comparing the levels of expression of a gene referred to as 20P1F12/TMPRSS2- which encodes the polypeptide of SEQ ID NO:2 wherein an "enhanced" level of the gene product compared to a comparable normal sample is evidence of prostate cancer.

The claims are not enabled because there is insufficient guidance and or objective evidence to one of ordinary skill in the art to use and or successfully practice the claimed invention with any predictability.

The specification teaches (page 4) that the present invention relates to methods and compositions for the diagnosis and therapy of prostate and colon cancer, derived from or based on a novel prostate-specific, androgen-regulated, serine protease termed 20P1F12/TMPRSS2. However, in comparing both the expression of 20P1F12/TMPRSS2 **RNA** and **protein** in both cancerous and normal prostate samples, the specification does not appear to teach "enhanced" levels that would clearly provide evidence of prostate cancer. For example, the specification teaches (page 85, line 19) that differential expression analysis by RT-PCR showed that the

20P1F12 gene is expressed at approximately equal levels in normal prostate compared to prostate cancer xenografts. Additionally, the specification teaches the expression of 20P1F12/TMPRSS2 in prostate cancer biopsies and surgical samples by immunohistochemical analysis. However, the specification fails to clearly differentiate the protein expression of 20P1F12/TMPRSS2 in normal versus cancerous prostate samples. The specification teaches (page 97, line 8) that analysis of 20 clinical specimens showed moderate to strong staining in the glandular epithelia of all normal prostate, PIN, and prostate cancer samples tested. Also, see Table 1, page 106 which indicates similar staining of human normal prostate tissue versus prostate cancer tissues with an anti-TMPRSS2 monoclonal antibody.

If a molecule such as 20P1F12/TMPRSS2 is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many proteins, including 20P1F12/TMPRSS2, are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polypeptide is present only in cancer tissue to the exclusion of normal tissue. Thus, in the absence of any correlation between the claimed peptides with any known disease or disorder, any information obtained from various expression profiles in both normal and diseased tissue only serves as the basis for further research on the observation itself. Therefore, absent evidence of the **protein's** expression including the correlation to a diseased state, one of skill in the art would not be able to predictably practice the claimed invention without undue experimentation.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

June 4, 2004

GARY NICKOL
PRIMARY EXAMINER